27. **(New)** An isolated polynucleotide molecule encoding a human vitamin D receptor (hVDR) isoform, said polynucleotide molecule comprising a nucleotide sequence having greater than 75% sequence identity to a nucleotide sequence of nucleotide residues 30-95 of SEQ ID NO:1.

28. **(New)** An isolated polynucleotide molecule encoding a human vitamin D receptor (hVDR) isoform, said polynucleotide molecule comprising a nucleotide sequence encoding the amino acid sequence MEWRNKKRSDWLSMVLRTAGVE.

29. **(New)** An isolated polynucleotide molecule comprising 10 or more contiguous nucleotides of SEQ ID NO:1 or a polynucleotide having greater than 95% sequence identity to SEQ ID NO:1.

REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 1-24 and 26-29 are pending after entry of the amendments set forth herein.

Claims 1-4, 9-14 and 21-24 were examined. Claims 1-4, 9-14 and 21-24 were rejected. No claims were allowed.

Please replace claims 1-4, 9-14 and 21-24, and add new claims 26-29 with the clean version provided above.

Attached hereto is a marked-up version of the changes made to the figures, specification and claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**" The changes to the figures are shown in the "red sketches" submitted herewith as per 37 CFR §1.121(d).

The Figures are amended to provide for the renumbering of the separated panels as required by 37 CFR §1.84(U)(1) as well as to provide the sequence identification numbers as required by 37 CFR §1.821(d).

The application is amended to insert a substitute Sequence Listing (attached) according to 37 CFR § 1.825. The substitute Sequence Listing includes sequences presented in the figures as originally filed. A substitute CRF is submitted herewith.

The application is further amended to provide an abstract on a separate page as required by 37 CFR §1.72(b). Support for this amendment is found in the specification at, for example, page 1, lines 1-8.

Claims 1-4, 13, 14, and 21-24 are amended. Support for the amendments to claims 1-4 are found in the specification at, for example, page 7, lines 4-16. Claims 13 and 14 are amended in view of the amendment to the claim 1 from which these claims ultimately depend, which amendment rendered the original language of claims 13 and 14 unnecessary. Claims 21-24 are amended to delete subject matter withdrawn from consideration. All amendments are made herein without prejudice, without acquiescing to any rejection applied to the claims, and without intent to abandon any subject matter encompassed therein.

New claims 26 - 29 are added

Support for new claim 26 is found in, for example, claim 1 as originally filed.

Support for new claims 27 and 28 if found in the specification at, for example, page 8, lines 12-14; Fig. 1 (particularly panel C), and page 16, lines 11-13.

Support for new claim 29 is found in the specification at, for example, page 5, line 34-36, and page 7, lines 16-34; and page 11, lines 23-34;

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

No new matter has been added.

Statement Regarding the Sequence Listing

I hereby certify that the enclosed Sequence Listing is being submitted under 37 CFR §§ 1.821(c) and (e) in paper and computer readable form (Compact Disk labeled 'CRF').

As required by 37 CFR 1.821(f), I hereby state that the content of the paper and computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(c) and (e) are the same. The Computer Readable Format (CRF), being submitted under 37 CFR §§ 1.52(e) and 1.824, is formatted on IBM-PC, the operating system compatibility is MS-Windows and the file listing is:

Seqlist.txt 29.4 KB created January 23, 2003.

I hereby certify that the enclosed submission includes no new matter. The Sequence Listing was prepared with the software FASTSEQ, and conforms to the Patent Office guidelines. Applicant respectfully submits that the subject application is in adherence to 37 CFR §§ 1.821-1.825.

Objections to the specification and drawings (paragraphs 1-6 of the Office Action)

The Office Action in paragraphs 1-6, pages 2-3 reviews the pending claims and the amendments entered, and kindly points out to applicants several informalities of the application as filed. Each of these are addressed below.

1) Entry of amendments

Applicants thank the Examiner for acknowledging entry of the amendment requested in Paper No. 8, filed February 11, 2002. However, it appears that the amendment to page 11, lines 31 and 32 requested in the document entitled "Amendments and Statement Under 37 CFR §1.821(f)" (filed at the time of filing of the instant application) were not entered (see below). Applicants request clarification in the next action as to whether these amendments were entered and, if not, applicants will re-present the request for the amendment in the next response.

2) The drawings - 37 CFR §1.821(d)

The drawings were objected to as lacking sequence identifiers. The replacement drawings submitted herewith should obviate this objection.

3) The specification -- 37 CFR §1.821(d)

The specification was objected to since the specification appeared to lack sequence identifiers as required by 37 CFR § 1.821(d), and particularly with respect to the primer sequences at page 11, lines 31 and 32. However, as noted above, in an amendment filed at the time of filing the instant application requested amendment of the specification to recite that the appropriate sequence identifiers of (SEQ ID NO:13) and (SEQ ID NO:14) be entered after "5'" at each of page 11, line 31 and page 11, lines 32. Since applicants are hesitant to create confusion on this matter, applicants respectfully request that the Examiner advise as to whether this amendment was received and entered. If not, applicants will gladly again request this amendment to the specification in the next response.

4) The specification and drawings-- 37 CFR § 1.84(U)(1)

The specification and drawings were objected since partial views of a drawing intended to form one complete view, when contained on several sheets, must be identified by the same number followed by a capital letter. The Examiner kindly reminded applicants that any amendment to the drawings in this regard would also require similar amendment of the specification to provide the corrected figure numbers. The amended drawings submitted herewith address this objection, and the specification is amendment accordingly.

5) The specification -- 37 CFR §1.72(b)

The specification was objected to as it lacks an abstract on a separate page. This objection is addressed by the amendment to enter the abstract as required.

6) Information Disclosure Statement

The Examiner kindly reminded applicants that listing of references in the specification is not a proper Information Disclosure Statement.

First, applicants note that an Information Disclosure Statement was filed at the time of filing of the instant application in order to ensure that those references cited in the International Search Report are made of record in the instant application. Applicants request consideration of the Information Disclosure Statement, and that the Examiner indicate consideration of the references cited therein by providing a copy of the initialed Form 1449 with the next action. Should the Examiner require another copy of the Information Disclosure Statement, he is welcome to contact the undersigned at the number provided.

Applicants submit herewith an Information Disclosure Statement to cite those references not already cited in the earlier filed Information Disclosure Statement, which references are listed on page 19 of the specification.

Restriction Requirement Made Final (Office Action paragraph 7)

First, applicants note that claim 25 was not among the claims considered in the restriction requirement set out in the Office Action mailed December 12, 2001. Since claim 25 was dependent upon claim 5, claim 5 is in a non-elected group, and the current Office Action treats claim 25 as being withdrawn, applicants are treating claim 25 as if it were included in the same restriction group as claim 5.

Applicants acknowledge that the Office has made the restriction requirement final, and particular with respect to the restriction of a polynucleotide into a group separate from the complement of that same polynucleotide. Applicants respectfully submit that examination of a polynucleotide and its complement should place no undue burden on the examination process, since a search for art relevant to a given sequence would likely also identify art relevant to the complement of the sequence. Further, there exist numerous instances in which the Office has, in the past, regarded a polynucleotide and its complement as capable of examination within a single application. For example, numerous patents have issued with language that recite a particular polynucleotide "or a complement thereof." See, for example, U.S. Pat. Nos. 6,465,631; 6,465,632; 6,465,717; 6,465,238; and 6,465,232. A search of the USPTO full-text database using the search strategy ACLM/"or complement thereof" and (ACLM/polynucleotide$ or ACLM/"nucleic acid" or ACLM/DNA) identified over 1,400 issued U.S. patents.

Furthermore, there is no undue burden on the Office to examine a polynucleotide and its complement together -- art disclosing a double stranded DNA relevant to one strand would be relevant to the complementary strand.

Nevertheless, Applicants understand that at this stage in the proceedings the restriction requirement is deemed final and thus examination now proceeds with the elected claims. However, Applicants expressly reserve their right under 37 CFR §1.144 to petition the Commissioner to review the restriction requirement. Applicants note that a petition may be deferred until after final action or notice of allowance (although not after appeal).

Accordingly, although maintained as pending, claims 5-6, 15-20 and 25 are presently withdrawn from consideration.

Objections based on improper Markush groups (Office Action paragraph 8)

Claim 1 was objected to as reciting improper Markush Groups on the grounds that a polynucleotide and its complement lack a common utility which is based upon a shared structural feature. Claims 21 and 24 were objected to as encompassing sequences of non-elected polynucleotides. This rejection is traversed as applied and as it may be applied to the pending claims.

Solely in the interest of maintaining applicants' rights to petition the restriction requirement as discussed above, claim 1 is amended to remove reference to the complement of the recited sequence, but new claim 26 is added to encompass this subject matter.

Claims 21-24 are amended so as to be directed to the elected polynucleotide, which comprises SEQ ID NO:1.

The Examiner is thus requested to withdraw this rejection of the pending claims presently under consideration.

Overview of the Subject Matter of the Claims -- VDR Isoform-Encoding Polynucleotides Having a Nucleotide Sequence of Exon1d

Before turning to the rejections of the claims under §112, ¶1 and §112, ¶2, applicants thought it may prove helpful to the Examiner to provide a brief overview of the claimed invention.

The inventors have discovered a novel exon -- exon1d -- that is differentially spliced to form novel human vitamin D receptor (hVDR) isoforms. As illustrated in Fig. 1, panel C, when present in a splice product, exon1d provides for a distinct N-terminal amino acid sequence as exemplified in transcripts 6 and 9. This N-terminal, 22 amino acid sequence is MEWRNKKRSDWLSMVLRTAGV. A 24th amino acid residue can be encoded as a result of joining of the 3' end of exon1d to the 5' end of the next exon in the sequence.

SEQ ID NO:1 provides a nucleotide sequence of exon1d, which sequence includes a 5'untranslated region and a coding region for the 22 amino acid sequence. The coding region begins at nucleotide residue 30 (see, e.g., Fig. 6A). When spliced to another exon, the 96th nucleotide residue of SEQ ID NO:1 provides for the first nucleotide of the codon for the next amino acid in the polypeptide, with the adjacent exon providing the 2nd and 3rd nucleotides of the codon (see, e.g., Fig. 6A).

With this overview in mind, applicants now turn to the remaining rejections.

Rejection under §112, ¶1 -- Written Description (Office Action paragraph 9)

Claims 1-4 and 9-14 were rejected as containing subject matter which was not described in the specification in such as way as to demonstrate to the ordinarily skilled artisan that the inventors, at the time of the application was filed, had possession of the claimed invention. This rejection is traversed as applied and as it may be applied to the pending claims.

Applicants note that the objected language is specifically defined in the specification. "Substantially corresponds" is defined at page 7, lines 4-11 to mean that the nucleotide sequence encompasses "minor variations in the nucleotide sequence which due to the degeneracy in the DNA code do not result in a substantial change in the encoded protein."

"Functionally equivalent" is defined "to encompass nucleotide sequence variants of up to 5% sequence divergence (i.e. retaining 95% or more sequence identity) which encode VDR isoforms of substantially equivalent biological activity(ies) as said VDR isoform).

As discussed in the overview above, SEQ ID NO:1 not only facilitates alternative splicing, but also encodes a 22 amino acid sequence of hVDR. The ordinarily skilled artisan would recognize that the nucleotide sequence variations that are due to the degeneracy of the genetic code means that the nucleotide sequence can vary in the 3rd nucleotide of a codon corresponding to an amino acid encoded by the polynucleotide. By providing an amino acid sequence, and reminding the ordinarily skilled artisan that such sequence variations exist, the artisan would readily understand which of these nucleotides is "critical to the function of that polynucleotide and those bases which are expendable", contrary to the assertion in the Office Action (page 8). The specification need not identify an analogous polynucleotide in the prior art to SEQ ID NO:1 in view of this understanding in the art. This is not to imply, of course, that this is the only type of nucleotide sequence variations the ordinarily skilled artisan would recognize, but rather is merely exemplary and provides for a large number of species of the claimed invention.

Without conceding as to the correctness of the grounds for rejection, claims 1-4 are amended to delete the language "substantially corresponds or is functionally equivalent to" and replace this language with that provided in the definitions above.

Withdrawal of this rejection is respectfully requested.

Rejection under §112, ¶1 -- Enablement (Office Action paragraph 10)

Claims 1-4 and 9-14 were rejected as containing subject matter which was not described in the specification in such as way as to enable the ordinarily skilled artisan to make and use the invention. This rejection is traversed as applied and as it may be applied to the pending claims.

As noted above, the terms "substantially corresponds" and "functionally equivalent" are defined in the specification. Applicants respectfully note that these definitions each require not only that biological activity of the encoded protein is retained, but also set additional boundaries on the scope of these terms -- specifically by requiring that "substantially corresponds" mean nucleotides that have sequence variation due to the degeneracy of the genetic code and requiring that "Functionally equivalent" sequence retain 95% or more sequence identity. Such polynucleotides can be readily made with the guidance provided in the specification, and thus are fully enabled.

However, without conceding as to the correctness of the grounds for rejection, claims 1-4 are amended to delete the language "substantially corresponds or is functionally equivalent to", replacing this language with that provided in the definitions above

Withdrawal of this rejection is respectfully requested.

Rejection under §112, ¶1 -- Enablement (Office Action paragraph 11)

Claims 21-24 were rejected as containing subject matter which was not described in the specification in such as way as to enable the ordinarily skilled artisan to make and use the invention. This rejection is traversed as applied and as it may be applied to the pending claims. This rejection is respectfully traversed.

First, applicants again note that, without conceding as to the correctness of the grounds for rejection, the claims are amended to delete the language "substantially corresponds or is functionally equivalent to", and the language replaced with that of the definitions of these terms.

Turning to the instant rejection, the Office Action notes that "whereas one could readily make a polynucleotide having at least 75% sequence identity to SEQ IDNO:1, the only specific utility disclosed for the claimed polynucleotide is in a process of producing alternatively spliced forms of a human vitamin D receptor, and the only polynucleotide described in the instant specification which functions in this capacity is SEQ ID NO:1."

Applicants agree that the ordinarily skilled artisan could make a polynucleotide having at least 75% sequence identity to SEQ IDNO:1 when provided with the instant specification. However, applicants respectfully note that the utility of SEQ ID NO:1 is not limited to providing for production of alternatively spliced forms of a hVDR.

As noted in the overview above, SEQ ID NO:1 contains a sequence coding for 22 amino acids of hVDR. When present in a splice variant, these 22 amino acids can be present at the N-terminus of the hVDR polypeptide. SEQ ID NO:1 therefore also has utility in that it provides for an N-terminal amino acid sequence of hVDR isoforms containing exon1d.

The ordinarily skilled artisan would recognize that, due to the degeneracy of the genetic code, polynucleotides that encode the same amino acid can have different nucleotide sequences. Each of the amino acids in the 22 amino acid sequence -- except for methionine -- have more than one codon, which codons differ in the third nucleotide. If a different codon were used for each of the 21 amino acids (the codon for methionine would be the same), the nucleotide sequence could differ by about 33%, i.e., the nucleotide sequence could be as little as 66% identical to SEQ ID NO:1. This latter concept --

nucleotide sequences that differ due to the degeneracy of the genetic code -- is further captured by the use of the language "having a nucleotide sequence encoding an amino acid sequence of exon 1d."

Thus, the ordinarily skilled artisan would recognize that polynucleotides of claims 21-24 would have utility in addition to production of splice variants -- and that these polynucleotides are useful in producing the amino acid sequence of exon1d.

Withdrawal of this rejection is respectfully requested.

Rejection under §112, ¶2 (Office Action paragraph 12)

Claims 1-4, 9-14 and 24 were rejected as being indefinite, particularly with respect to the language "functionally equivalent" and "substantially corresponds". This rejection is traversed as applied and as it may be applied to the pending claims.

Applicants respectfully submit that the objected language is well-defined in the specification, as discussed repeatedly and in detail above. Applicants further respectfully note that the statement in the Office Action that "Figure 1 . . . appears to indicate that SEQ IDNO:1 lies in a 5' non-coding region of a vitamin D gene and, therefore, encodes nothing" (page 9) is not completely accurate. Applicants respectfully note that, as discussed in the overview above, SEQ ID NO:1 contains both a 5' non-coding region and a coding sequence for the N-terminal portion of hVDR isoform polypeptides. Applicants hope that the discussion in the overview will facilitate the Office's reading of Figure 1 in light of the specification.

Without conceding as to the correctness of the grounds for rejection, the claims are amended to delete the language "substantially corresponds or is functionally equivalent to", and the language replaced with that of the definitions of these terms.

Withdrawal of this rejection is respectfully requested.

Claims free of prior art

Applicants gratefully acknowledge the Examiner's indication that the claims are free of the prior art with respect to a polynucleotide comprising SEQ ID NO:1.

Conclusion

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RICE-014.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Jan 23, 2003

By: _____
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Delete pages 20-28 of the specification (the Sequence Listing).

Renumber pages 29-33 as pages 20-24.

Insert new page 25 entitled "Abstract of the Invention" after newly renumbered page 24 (after the claims).

Insert the enclosed document entitled "Sequence Listing", numbered beginning with page 1 after the abstract.

Replace the paragraph bridging pages 7-8 with the following:

~~FIG.1. (A)~~ **FIG. 1A** Human VDR gene locus. Four overlapping cosmid clones were isolated from a human lymphocyte genomic library (Stratagene) and directly sequenced. Clone J5 extends from the 5' flanking region to intron 2; AE, from intron 1b to intron 5; D2, from intron 3 to the 3' UTR; WE, from intron 6 through the 3' flanking region. Sequence upstream of exon 1f was obtained by anchored PCR from genomic DNA. ~~(B)~~ **FIG. 1B** Structure of hVDR transcripts. Transcripts 1–5 originate from exon 1a. Transcript 1 corresponds to the published cDNA (1). Transcripts 6–10 originate from exon 1d and transcripts 11–14 originate from exon 1f. Boxed numbers indicate the major transcript (based on the relative intensities of the multiple PCR products) within each exon-specific group of transcripts generated with a single primer set. While all transcripts have a translation initiation codon in exon 2, exon 1d transcripts have the potential to initiate translation upstream in exon 1d, with transcripts 6 and 9 encoding VDR proteins with extended N termini. ~~(C)~~ **FIG. 1C** N-terminal variant proteins encoded by novel hVDR transcripts. Transcript 1 corresponds to the published cDNA sequence (1) and encodes the 427-aa hVDR protein. Transcripts 6 and 9 code for a protein with an extra 50 aa or 23 aa, respectively, at the N-terminal. The 23 aa of the hVDR A/B domain are shown in bold.

Replace the paragraphs at page 9 lines 17 to 35 with the following:

~~FIG. 5.~~ **FIGS. 5A-5D.** Provides the nucleotide sequence corresponding to transcript 6 (see figure 1) (SEQ ID NO: 2), together with the predicted amino acid sequence (SEQ ID NO: 9) of the encoded protein. Nucleotides 1-96 correspond to exon 1d; nucleotides 97-1463 correspond to exons 1c to the stop codon in exon 9 (or nucleotides -83-1283 of the hVDR cDNA (1)).

~~FIG. 6.~~ **FIGS. 6A-6D.** Provides the nucleotide sequence corresponding to transcript 9 (see figure 1) (SEQ ID NO: 3), together with the predicted amino acid sequence (SEQ ID NO: 10) of the encoded protein. Nucleotides 1-96 correspond to exon 1d; nucleotides 97 - 1382 correspond to exon 2 to the stop codon in exon 9 (or nucleotides -2 - 1283 of the hVDR cDNA (1)).

~~FIG. 7.~~ **FIGS. 7A-7D.** Provides the nucleotide sequence corresponding to transcript 10 (see figure 1) (SEQ ID NO: 4), together with the predicted amino acid sequence (SEQ ID NO: 11) of the encoded protein. Nucleotides 1-96 correspond to exon 1d; nucleotides 97-244 correspond to exon 2; nucleotides 245-396 correspond to intronic sequence immediately 3' to exon 2; nucleotides 397-1534 correspond to exons 3 to the stop codon in exon 9 (or nucleotides 146-1283 of the hVDR cDNA (1)).

Replace the paragraph beginning at page 10, line 1 with the following:

~~FIG. 8.~~ **FIGS. 8A-8D.** Provides the nucleotide sequence corresponding to transcript 11 (see figure 1) (SEQ ID NO: 7), together with the predicted amino acid sequence (SEQ ID NO: 12) of the encoded protein. Nucleotides 1-207 correspond to exon 1f; nucleotides 208-1574 correspond to exon 1c to the stop codon in exon 9 (or nucleotides -83-1283 of the hVDR cDNA (1)).

Claims 26-29 have been added.

1. **(Amended)** An isolated polynucleotide molecule encoding a human vitamin D receptor (hVDR) isoform, said polynucleotide molecule comprising **i)** a nucleotide sequence **having 95% or more sequence identity to a nucleotide sequence** ~~which comprises a sequence that substantially corresponds or is functionally equivalent to that~~ of exon 1d of the human VDR gene**, or fragment thereof, or ii) a nucleotide sequence encoding an amino acid sequence of exon 1d or fragment thereof** ~~or a sequence complementary thereto~~.

2. **(Amended)** A polynucleotide molecule according to claim 1, wherein said nucleotide sequence further includes

i) a nucleotide sequence having 95% or more sequence identity to a nucleotide sequence of, or encoding an amino acid sequence of, exon 1b or fragment thereof;

ii) a nucleotide sequence having 95% or more sequence identity to a nucleotide sequence of, or encoding an amino acid sequence of, exon 1c or fragment thereof; or

iii) a nucleotide sequence having i) and ii)

~~sequence that substantially corresponds or is functionally equivalent to that of exon 1b and/or exon 1c~~.

3. **(Amended)** A polynucleotide molecule according to claim 1, wherein the nucleotide sequence includes:

(i) a sequence **having 95% or more sequence identity to a nucleotide sequence of, or encoding an amino acid sequence of,** ~~that substantially corresponds or is functionally equivalent to that~~ of exons 1d, 1c and 2-9 and encodes a VDR isoform of approximately 477 amino acids,

(ii) a sequence **having 95% or more sequence identity to a nucleotide sequence of, or encoding an amino acid sequence of,** ~~that substantially corresponds or is functionally equivalent to that~~ of exons 1d and 2-9 and encodes a VDR isoform of approximately 450 amino acids, or

(iii) a sequence **having 95% or more sequence identity to a nucleotide sequence of, or encoding an amino acid sequence of,** ~~that substantially corresponds or is functionally equivalent to that~~ of exons 1d and 2-9 and further includes a 152bp intronic sequence and encodes a truncated VDR isoform of approximately 72 amino acids.

4. **(Amended)** A polynucleotide molecule according to claim 1, wherein the **polynucleotide comprises a** nucleotide sequence **having 95% or more sequence identity to a nucleotide sequence of, or encoding an amino acid sequence encoded** by, ~~that substantially corresponds to that shown as~~ SEQ ID NO:2, SEQ ID NO:3 or SEQ ID NO:4.

13. **(Amended)** A method of producing a VDR or VDR isoform **polypeptide, or a fragment thereof,** ~~functionally equivalent fragments thereof~~, comprising culturing a host cell of claim 10 under conditions enabling the expression of the polynucleotide molecule and, optionally, recovering the VDR or VDR isoform **polypeptide** ~~or functionally equivalent fragments thereof~~.

14. **(Amended)** A method according to claim 13, wherein the VDR or VDR isoform **polypeptide, or a fragment thereof,** ~~or functionally equivalent fragments thereof are~~ **is** expressed onto the host cell membrane or other sub-cellular compartment.

21. **(Amended)** An isolated polynucleotide molecule comprising a nucleotide sequence showing greater than 75% sequence identity to ÷

~~(i) 5'CGACCTTGGCGGTGAGCCTGGGGACAGGGGTGAGGCCAGAGACGGACG GACGCAGGGGCCCGGCCCAAGGCGAGGGAGAACAGCGGCACTAAGGCAGA AAGGAAGAGGGCGGTGTGTTCACCCGCAGCCCAATCCATCACTCAGCAAC TCCTAGACGCTGGTAGAAAGTTCCTCCGAGGAGCCTGCCATCCAGTCGTG CGTGCAG3' (SEQ ID NO: 5)~~

~~(ii) 5'AGGCAGCATGAAACAGTGGGATGTGCAGAGAGAAGATCTG GGTCCAGTAGCTCTGACACTCCTCAGCTGTAGAAACCTTGACAACTCTGC ACATCAGTTGTACAATGGAACGGTATTTTTTACTCTTCATGTCTGAAAAG GCTATGATAAAGATCAA3' (SEQ ID NO: 6), or~~

~~(iii)~~ GTTTCCTTCTTCTGTCGGGGCGCCTTGGCATGGAGTGGAGGAATAAGAAA AGGAGCGATTGGCTGTCGATGGTGCTCAGAACTGCTGGAGTGGAGG3' (SEQ ID NO:1)

22. **(Amended)** An isolated polynucleotide molecule comprising a nucleotide sequence showing greater than 85% sequence identity to ÷

~~(i) 5'CGACCTTGGCGGTGAGCCTGGGGACAGGGGTGAGGCCAGAGACGGACG GACGCAGGGGCCCGGCCCAAGGCGAGGGAGAACAGCGGCACTAAGGCAGA AAGGAAGAGGGCGGTGTGTTCACCCGCAGCCCAATCCATCACTCAGCAAC TCCTAGACGCTGGTAGAAAGTTCCTCCGAGGAGCCTGCCATCCAGTCGTG CGTGCAG3' (SEQ ID NO: 5)~~

~~(ii) 5'AGGCAGCATGAAACAGTGGGATGTGCAGAGAGAAGATCTG GGTCCAGTAGCTCTGACACTCCTCAGCTGTAGAAACCTTGACAACTCTGC ACATCAGTTGTACAATGGAACGGTATTTTTTACTCTTCATGTCTGAAAAG GCTATGATAAAGATCAA3' (SEQ ID NO: 6), or~~

~~(iii)~~ GTTTCCTTCTTCTGTCGGGGCGCCTTGGCATGGAGTGGAGGAATAAGAAA AGGAGCGATTGGCTGTCGATGGTGCTCAGAACTGCTGGAGTGGAGG3' (SEQ ID NO:1)

23. **(Amended)** An isolated polynucleotide molecule comprising a nucleotide sequence showing greater than 95% sequence identity to÷

~~(i) 5'CGACCTTGGCGGTGAGCCTGGGGACAGGGGTGAGGCCAGAGACGGACG GACGCAGGGGCCCGGCCCAAGGCGAGGGAGAACAGCGGCACTAAGGCAGA AAGGAAGAGGGCGGTGTGTTCACCCGCAGCCCAATCCATCACTCAGCAAC TCCTAGACGCTGGTAGAAAGTTCCTCCGAGGAGCCTGCCATCCAGTCGTG CGTGCAG3' (SEQ ID NO: 5)~~

~~(ii) 5'AGGCAGCATGAAACAGTGGGATGTGCAGAGAGAAGATCTG GGTCCAGTAGCTCTGACACTCCTCAGCTGTAGAAACCTTGACAACTCTGC ACATCAGTTGTACAATGGAACGGTATTTTTTACTCTTCATGTCTGAAAAG GCTATGATAAAGATCAA3' (SEQ ID NO: 6), or~~

(iii) GTTTCCTTCTTCTGTCGGGGCGCCTTGGCATGGAGTGGAGGAATAAGAAA AGGAGCGATTGGCTGTCGATGGTGCTCAGAACTGCTGGAGTGGAGG3' (SEQ ID NO:1)

24. **(Amended)** An isolated polynucleotide molecule comprising a nucleotide sequence **of** ~~substantially corresponding to:~~

~~(i) 5'CGACCTTGGCGGTGAGCCTGGGGACAGGGGTGAGGCCAGAGACGGACG GACGCAGGGGCCCGGCCCAAGGCGAGGGAGAACAGCGGCACTAAGGCAGA AAGGAAGAGGGCGGTGTGTTCACCCGCAGCCCAATCCATCACTCAGCAAC TCCTAGACGCTGGTAGAAAGTTCCTCCGAGGAGCCTGCCATCCAGTCGTG CGTGCAG3' (SEQ ID NO: 5)~~

~~(ii) 5'AGGCAGCATGAAACAGTGGGATGTGCAGAGAGAAGATCTG GGTCCAGTAGCTCTGACACTCCTCAGCTGTAGAAACCTTGACAACTCTGC ACATCAGTTGTACAATGGAACGGTATTTTTTACTCTTCATGTCTGAAAAG GCTATGATAAAGATCAA3' (SEQ ID NO: 6), or~~

~~(iii)~~ GTTTCCTTCTTCTGTCGGGGCGCCTTGGCATGGAGTGGAGGAATAAGAAA AGGAGCGATTGGCTGTCGATGGTGCTCAGAACTGCTGGAGTGGAGG3' (SEQ ID NO:1)